

Remarks

I. The Office Action

The November 14, 2006 final Office Action (the "Office Action") in this application:

1. rejected claims 1 and 8-9 under 35 U.S.C. 103(a) as unpatentable over Anderson et al. in view of Sugiyama et al.

Applicants respond to the Office Action as follows.

II. Rejection of Claims 1, 8 and 9 under 35 U.S.C. 103(a)

The Office Action rejects claims 1, 8 and 9 under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. in view of Sugiyama. Respectfully, the rejection is in error and should be withdrawn.

Firstly, there is no motivation to combine Anderson et al. and Sugiyama, as detailed below.

A review of the entirety of Anderson et al. reveals that this disclosure is directed to reporting on the efficacy and adverse effects of repeated botulinum toxin injections in neck muscles of patients suffering from spasmodic torticollis (see Summary), also known as cervical dystonia. Anderson et al. describes the long term benefit provided to patients subjected to repeated injections of botulinum toxin type A. In fact, Anderson et al. is so impressed with the results of repeatedly administering botulinum toxin type A to these patients that it is concluded that "...botulinum toxin injection *must* now be considered the mainstay of therapy for spasmodic torticollis." (page 528, lines 65-67, emphasis ours). It is important to note that the botulinum toxin injections in Anderson et al. are all injections of only botulinum toxin type A.

Significantly, Anderson *does not* teach, mention or suggest the use of *any* botulinum toxin other than type A botulinum toxin. This is not surprising, particularly in light of the glowing success that Anderson et al. reports for the regimen disclosed (see page 525, Table 1), and that patients should expect "a 90% chance of some improvement" (page 528, lines 49-52) following treatment (i.e. multiple injections of botulinum toxin type A).

Even more particularly, Anderson et al. does not teach or suggest the use of *any combination* of botulinum toxin types, let alone toxin types A with B or A with E, where an amount of each selected neurotoxin provides the combination

effective in providing enhancement of relief of muscle contraction for a short duration and also provides long term relief for treating a neuromuscular condition or disorder, as presently claimed.

Accordingly, there is no reason and nothing in this reference that would motivate, teach or suggest to one of ordinary skill in the art to look to any further methods of treatment other than the disclosed, repeated administration of botulinum toxin type A, or to contemplate simultaneous administration of *combinations* of various botulinum toxins, as Anderson et al. clearly indicates that the disclosed mode of treatment, i.e. repeated administration of only botulinum toxin type A, is reported to be so effective and successful that it should be considered "...the mainstay of therapy for spasmodic torticollis." (page 528, lines 65-67). Thus, Anderson et al. clearly *teaches away* from the use of any other method of treatment, including the simultaneous administration of selected combinations of botulinum toxin types, such as the instantly claimed botulinum toxin type A in combination with botulinum toxin type B or E.

It has been noted that that references that teach away from a claimed invention cannot serve to create a prima facie case of obviousness or used to rejected a claim. (In re Gurley, 27 F.3d 551, 553, 31 USPQ2d 1131, 1132 (Fed. Cir. 1994) *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983) ("...the district court erred in...disregarding disclosures in the references that diverge from and teach away from the invention at hand." 220 USPQ at 311). Accordingly, Anderson et al. cannot be utilized in asserting a prima facie case of obviousness.

While the Office Action urges that it is the combination of the cited references that teaches the claimed invention, the Office Action fails to point out how the respective disclosures teach, motivate or suggest to one of ordinary skill in the art *their combination* and the subsequent modification of their disclosures, to arrive at the claimed invention, particularly since Anderson et al. and

Sugiyama are such disparate types of disclosures (a report on therapeutic use of botulinum toxin type A and an academic botulinum toxin structural review article, respectively), and both fail to teach or suggest the use of simultaneous administration of differing botulinum toxin types, particularly the claimed combination of botulinum toxin types (A+B and A+E).

Sugiyama is a review article published in a microbiology journal which discusses various pharmacological aspects of the *Clostridium botulinum* neurotoxin serotypes including toxicities, structural and binding aspects. *Importantly*, there is no disclosure in Sugiyama of any *therapeutic or clinical use of combinations* of botulinum toxin types. In spite of the Office Action's assertion, the simple disclosure of various botulinum toxin type characteristics does not provide motivation for one of ordinary skill in the art to combine these teachings (aspects of individual toxin types) with the teachings of Anderson et al. (administration of botulinum toxin type A to treat spasmodic dystonia).

It has been held that "... that a person of ordinary skill in the art must not *only* have had *some motivation* to combine the prior art teachings, but *some motivation* to combine the prior art teachings in the *particular manner claimed*. See, e.g., *In re Kotzab*, 217 F.3d 1365, 1371 (Fed. Cir. 2000) (emphasis added). As stated above, Anderson et al. does even not disclose the use of *any* botulinum toxin type other than type A (and in fact teaches away from the use of other types, as discussed above) let alone a combination of botulinum toxin types and *thus lacks the requisite motivation* to combine itself with any other disclosure. Sugiyama similarly does not disclose, teach or suggest any *therapeutic or clinical use of combinations* of botulinum toxin types. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Although a prior art device "may be capable of being modified to run the way the

apparatus is claimed, there must be a suggestion or motivation in the reference to do so." 916 F.2d at 682.

Clearly, and even if erroneously combined through hindsight analysis in an attempt to reconstruct the claimed invention, there is no teaching or suggestion in Anderson et al. and Sugiyama, either individually or in combination, to "administer simultaneously" (all instant claims) a botulinum toxin type A and a type B or E botulinum toxin. Additionally, there is no teaching or suggestion, either individually or in a combination of Anderson and Sugiyama, of administering simultaneously botulinum toxins A with type B or E to achieve a desired effect and provide a short duration of that effect along with long term relief (all claims).

Additionally, the Office Action has failed to show where, specifically and in the cited references, it is shown or suggested that each of the recited neurotoxins is taught by the prior art to be useful for the same purpose in order to form a third composition to be used for *the very same purpose* at the earliest effective filing date of the instant application. For example, the claimed combination is to provide an amount of each selected neurotoxin such that the combination is effective in providing an enhancement of relief of muscle contraction for a short duration, and long term relief for treating the neuromuscular disorder or condition.

Furthermore, both Anderson et al. and Sugiyama, alone or in combination, are silent with respect to a method for treating a patient utilizing the claimed combination of botulinum toxin type A and B, or A and E, in amounts selected such that the combination is effective in providing an enhancement of relief of muscle contraction for a short duration, wherein the duration of therapeutic activity is suitable for treatment of joint dislocations, relaxation for physical therapy, alleviation of muscle spasm, immobilization of a joint undergoing surgery and for prevention of muscle contractions prior to or after surgery (claim 8). The cited references, alone or on combination, are also silent with respect to a

combination of botulinum toxin type A and B, or A and E that provides a duration of therapeutic activity suitable for treating tendon and ligament alignment repair, treatment of scoliosis and spasm of sphincter muscles (claim 9). Thus, these dependent claims are also allowable and nonobvious in light of the cited references

Thus, at least because: (a) there is no motivation to combine Anderson and Sugiyama; (b) Anderson et al. teaches away from the use of any botulinum toxins other than type A and logically, away from combinations of botulinum toxins; and (c) the combination of Anderson and Sugiyama does not disclose, teach or suggest the claimed invention, the rejection should be withdrawn.

VI. Conclusion

All issues raised in the Office Action have been addressed. Examination and allowance of claims 1 and 8, 9 is requested.

Respectfully submitted,

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